



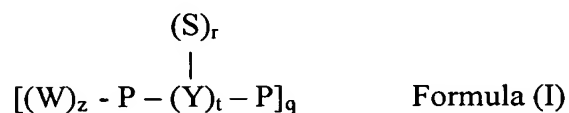
Appl. No. 10/029,988

Amendments to the claims:

This listing of claims will replace all prior versions and listing of claims in the application:

Listing of Claims:

Claim 1 (currently amended) An isolated $[[A]]$ human antibody multimer comprising at least a first and a second antigen binding fragment, wherein the at least first or second antigen binding fragment or both is capable of binding or cross-reacting with an epitope comprising the formula



Wherein:

W is any amino acid other than Aspartate and Glutamate

Y is an amino acid selected from the group consisting of Tyrosine, Asparagine, Serine and Threonine

P is independently selected from the group consisting of $(A)_m(A)_n(X)_u$, $(X)_u(A)_n(A)_m$, $(A)_n(X)_u(A)_m$, $(A)_n(A)_m(X)_u$, or $(X)_u(A)_m(A)_n$, and $(A)_m(X)_u(A)_n$

S is sulfate or a sulfated molecule

X is any amino acid except Aspartate, Glutamate, or Tyrosine

A is independently selected from the group consisting of any negatively charged amino acid, leucine, isoleucine, proline, phenylalanine, serine, and glycine

q is 1 to 6

z is 0, 1, or 2

r is 0 or 1

t is 1, 2 or 3

u is 0 to 2

n is 0 to 3

m is 0 to 3

wherein if n = 0 then m > 0; wherein if m = 0 then n > 0; wherein if q is 1, r is 1, and if q is > 1 at least one of Y is sulfated.

Claim 2 (previously presented) An antibody multimer of claim 1 wherein the first or second antigen binding fragment or both binds or cross reacts with the epitope in which:

W is Glycine,

Y further comprises a peptido conjugate of Tyrosine or a glyco conjugate of Asparagine, Serine or Threonine.

At least one A is Glutamate, γ Carboxy Glutamate or Aspartate

q is 1, 2, or 3.

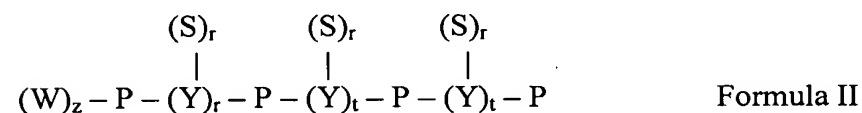
Claim 3 (previously presented) An antibody multimer of claim 2 wherein the first or second antigen binding fragment or both binds or cross reacts with the epitope in which:

Y is a peptido conjugate of Tyrosine

q is 3

r is 1.

Claim 4 (currently amended) A isolated human antibody multimer comprising at least a first and second antigen binding fragment, wherein the first or second antigen binding fragment or both is capable of binding or cross-reacting with an epitope comprising the formula



Wherein:

W is any amino acid other than Aspartate and Glutamate

Y is an amino acid selected from the group consisting of Tyrosine, Asparagine, Serine and Threonine

P is independently selected from the group consisting of $(A)_m(A)_n(X)_u$, $(X)_u(A)_n(A)_m$, $(A)_n(X)_u(A)_m$, $(A)_n(A)_m(X)_u$, or $(X)_u(A)_m(A)_n$, and $(A)_m(X)_u(A)_n$

S is a sulfate or a sulfated molecule

X is any amino acid except Aspartate, Glutamate or Tyrosine

A is independently selected from the group consisting of any negatively charged amino acid, leucine, isoleucine, proline, phenylalanine, serine, and glycine

z is 0, 1, or 2

r is 0 or 1

t is 1, 2 or 3

u is 0 to 2

n is 0 to 3

m is 0 to 3

wherein if $n = 0$ then $m > 0$; wherein if $m = 0$ then $n > 0$; wherein at least one Y is sulfated.

Claim 5 (previously presented) An antibody multimer of claim 4 wherein the first or second antigen binding fragment or both binds or cross reacts with the epitope in which:

W is Glycine

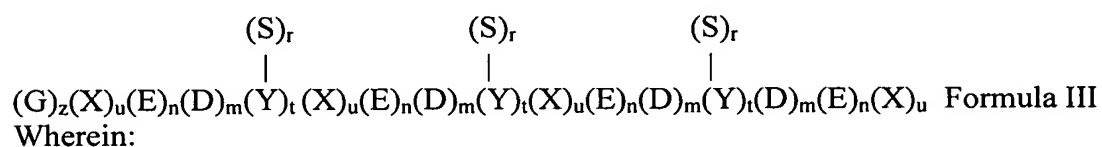
Y further comprises a peptido conjugate of Tyrosine or a glyco conjugate of Asparagine, Serine or Threonine

at least one A is Glutamate, γ Carboxy Glutamate, Aspartate, Leucine, Isoleucine, Proline, Phenylalanine, Serine, or Glycine.

Claim 6 (previously presented) An antibody multimer of claim 4 wherein the first or second antigen binding fragment or both binds or cross reacts with the epitope in which:

Y is a peptido conjugate of Tyrosine
and
r is 1.

Claim 7 (currently amended) An isolated [[A]] human antibody multimer comprising at least a first and second antigen binding fragment, wherein the at least first or second antigen binding fragment or both is capable of binding or cross-reacting with an epitope comprising the formula (SEQ ID NO:216):



G is Glycine
E is Glutamate
D is Aspartate
Y is Tyrosine
S is sulfate or a sulfated molecule
X is any amino acid except Glycine, Glutamate, Aspartate, or Tyrosine
z is 0, 1, or 2
t is 1, 2 or 3
r is 0 or 1
u is 0 to 2
n is 0 to 3
m is 0 to 3

wherein at least one Y is sulfated; wherein if $n = 0$ then $m > 0$; wherein if $m = 0$ then $n > 0$.

Claim 8 (original) An antibody multimer of claim 7 wherein the first or second antigen binding fragment or both binds or cross reacts with the epitope in which r is 1.

Claim 9 (previously presented) An antibody multimer of claim 1 wherein the multimer is a dimer, trimer or tetramer.

Claim 10 (original) An antibody multimer of claim 9 wherein the multimer is a dimer.

Claim 11 (original) A dimer of claim 10 wherein at least one of the first and second antigen binding fragments is selected from scFv fragments of Y1 and Y17.

Claim 12 (original) A dimer of claim 10 wherein the first and second antigen binding fragments are linked by a disulfide bridge.

Claim 13 (original) A dimer of claim 12 wherein the first and second antigen binding fragments are Y1-CysKAK.

Claim 14 (original) A dimer of claim 10 wherein the first and second antigen binding fragments are linked by a polypeptide linker of 5 to 20 amino acids.

Claim 15 (original) A dimer of claim 14 wherein the polypeptide linker comprises 5 amino acids.

Claim 16 (original) A dimer of claim 15 wherein the polypeptide linker is Gly₄Ser.

Claim 17 (original) An antibody multimer of claim 9 wherein the multimer is a trimer.

Claim 18 (original) A trimer of claim 17 comprising three antigen binding fragments, wherein at least one of the antigen binding fragments is a Y1 scFv fragment or Y17 scFv fragment.

Claim 19 (original) A trimer of claim 18 wherein the antigen binding fragments are linked by a polypeptide linker.

Claim 20 (original) A trimer of claim 19 wherein the polypeptide linker comprises 1 to 5 amino acids.

Claim 21 (original) An antibody multimer of claim 9 wherein the multimer is a tetramer.

Claim 22 (original) A tetramer of claim 21 comprising four antigen binding fragments, wherein at least one of the antigen binding fragments is a Y1 scFv fragment or Y17 scFv fragment.

Claim 23 (original) A tetramer of claim 22 wherein the antigen binding fragments are linked by a polypeptide linker.

Claim 24 (original) A tetramer of claim 23 wherein the polypeptide linker comprises 1 to 5 amino acids.

Claim 25 (original) A tetramer of claim 21 wherein the four antigen binding fragments form a complex through streptavidin-biotin association.

Claim 26 (original) An antibody multimer of claim 9 comprising identical antigen binding fragments.

Claim 27 (original) An antibody multimer of claim 9 wherein the at least first or second antigen binding fragment or both comprises a first hypervariable region comprising SEQ ID NO: 8.

Claim 28 (original) An antibody multimer of claim 9 wherein the at least first or second antigen binding fragment or both comprises a first hypervariable region comprising SEQ ID NO:20.

Claim 29 (original) An antibody multimer of claim 27 or 28 wherein the at least first or second antigen binding fragment or both has a second hypervariable region comprising SEQ ID NO: 115 and/ or a third hypervariable region comprising SEQ ID NO: 114.

Claim 30 (previously presented) An antibody multimer of any one of claims 1, 4, 7, 27, 28, 117, 118, 138, and 139 wherein the multimer is capable of binding to at least two different molecules selected from the group consisting of PSGL-1, fibrinogen gamma prime (γ'), GP1b α , heparin, lumican, complement compound 4 (CC4), interalpha inhibitor, and prothrombin.

Claim 31 (previously presented) An antibody multimer of any one of claims 1, 4, 7, 27, 28, 117, 118, 138, and 139 wherein the multimer is capable of binding to at least two different molecules selected from the group consisting of PSGL-1, fibrinogen gamma prime (γ'), GP1b α , heparin, lumican, complement compound 4 (CC4), interalpha inhibitor, and prothrombin and is capable of binding to at least one cell type selected from the group consisting of B-CLL cells, AML cells, multiple myeloma cells, and metastatic cells.

Claim 32 (previously presented) A dimer of claim 10, 100 or 121 comprising a first and second antigen binding fragment, wherein said first or second antigen binding fragment or both comprises a hypervariable region comprising the amino acid sequence of SEQ ID NO: 8 [Y1 CDR3]

Claim 33 (previously presented) A dimer of claim 10, 100 or 121 comprising a first and second antigen binding fragment, wherein said first or second antigen binding fragment or both comprise a hypervariable region comprising the amino acid sequence of SEQ ID NO: 20 [Y17 CDR3].

Claim 34 (previously presented) An antibody dimer of claim 32, wherein said first or second antigen binding fragment or both further comprises a second hypervariable region comprising the amino acid sequence of SEQ ID NO: 115 and/or a third hypervariable region comprising SEQ ID NO: 114.

Claim 35 (currently amended) An isolated human antibody multimer comprising a first and second antigen binding fragment, wherein said first or second antigen binding fragment or both is capable of cross-reacting with two or more epitopes, each epitope comprising one or more sulfated tyrosine residues and at least one cluster of two or more acidic amino acids, ; with the provisio that the antibody multimer is not a SZ2 antibody multimer nor a KPL1 antibody multimer.

Claim 36 (original) An antibody multimer of claim 35 wherein said multimer is capable of cross-reacting with PSGL-1.

Claim 37 (previously presented) An antibody multimer of claim 35 that binds to QATEYDYLDYDFLPETE (SEQ ID NO: 225) wherein at least one tyrosine residue is sulfated.

Claim 38 (original) An antibody multimer of claim 35 wherein the multimer is capable of cross-reacting with GP1b- α .

Claim 39 (previously presented) An antibody multimer of claim 35 that binds to DEGDTDLYDYYPEEDTEGD (SEQ ID NO: 218) wherein at least one tyrosine residue is sulfated.

Claim 40 (previously presented) An antibody multimer of claim 35 that binds to TDLYDYYPEEDTE (SEQ ID NO: 215) wherein at least one tyrosine residue is sulfated.

Claim 41 (previously presented) An antibody multimer of claim 35 that binds to DEGDTDLYDYYP (SEQ ID NO: 265) wherein at least one tyrosine residue is sulfated.

Claim 42 (previously presented) An antibody multimer of claim 35 that binds to YDYYPEE (SEQ ID NO: 266) wherein at least one tyrosine residue is sulfated.

Claim 43 (previously presented) An antibody multimer of claim 35 that binds to TDLYDYYP (SEQ ID NO: 267) wherein at least one tyrosine residue is sulfated.

Claim 44 (original) An antibody multimer of claim 35 wherein the multimer is capable of cross-reacting with fibrinogen gamma prime.

Claim 45 (previously presented) An antibody multimer of claim 44 that binds to EHPAETEDSLYPED (SEQ ID NO: 235) wherein at least one tyrosine residue is sulfated.

Claim 46 (original) An antibody multimer of claim 35 wherein the multimer is capable of cross-reacting with heparin.

Claim 47 (original) An antibody multimer of claim 35 wherein the multimer is capable of cross-reacting with complement 4 (CC4).

Claim 48 (original) An antibody multimer of claim 35 that is capable of cross-reacting with at least one cell selected from the group consisting of B-CLL cells, AML cells, multiple myeloma cells and metastatic cells.

Claim 49 (previously presented) A pharmaceutical composition comprising an antibody multimer according to any one of claims 1, 4, 7, 27, 28, 117, 118, 138, and 139.

Claim 50 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an effective amount to increase mortality of tumor cells or to increase the susceptibility of tumor cells to damage by an anti-cancer agent.

Claim 51 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an effective amount to inhibit growth and/or replication of leukemia cells.

Claim 52 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an effective amount to inhibit abnormal cell-cell, cell-matrix, platelet-matrix, platelet-platelet, and/or platelet-cell adhesion.

Claim 53 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an effective amount to increase the susceptibility of diseased cells to damage by anti-disease agents.

Claim 54 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an effective amount to increase the mortality of leukemia cells amount or to increase the susceptibility of leukemia cells to damage by anti-leukemia agents.

Claim 55 (previously presented) A pharmaceutical composition comprising an antibody multimer according to any one claims 1, 4, 7, 27, 28, 117, 118, 138, and 139 coupled to or complexed with an agent selected from the group consisting of anti-cancer, anti-metastasis, anti-leukemia, anti-disease, anti-adhesion, anti-thrombosis, anti-restenosis, anti-auto-immune, anti-aggregation, anti-bacterial, anti-viral, and anti-inflammatory agents.

Claim 56 (original) A pharmaceutical composition of claim 55 wherein the agent is selected from the group consisting of toxins, radioisotopes and pharmaceutical agents.

Claim 57 (original) A pharmaceutical composition of claim 55 wherein the agent is an anti-viral agent selected from the group consisting of acyclovir, ganciclovir and zidovudine.

Claims 58-60 (canceled)

Claim 61 (original) A pharmaceutical composition of claim 55 wherein the agent is an anti-adhesion/anti-aggregation agent selected from the group consisting of limaprost, clorcromene, and hyaluronic acid.

Claim 62 (previously presented) A pharmaceutical composition of claim 56 wherein the radioisotope is selected from the group consisting of gamma-emitters, positron-emitters, x-ray emitters, beta-emitters, and alpha-emitters.

Claim 63 (original) A pharmaceutical composition of claim 62 wherein the wherein the radioisotope is selected from the group consisting of $^{111}\text{indium}$, $^{113}\text{indium}$, $^{99\text{m}}\text{rhenium}$, $^{105}\text{rhenium}$, $^{101}\text{rhenium}$, $^{99\text{m}}\text{technetium}$, $^{121\text{m}}\text{tellurium}$, $^{122\text{m}}\text{tellurium}$, $^{125\text{m}}\text{tellurium}$, $^{165}\text{thulium}$, $^{167}\text{thulium}$, $^{168}\text{thulium}$, $^{123}\text{iodine}$, $^{126}\text{iodine}$, $^{131}\text{iodine}$, $^{133}\text{iodine}$, $^{81\text{m}}\text{krypton}$, $^{33}\text{xenon}$, $^{90}\text{yttrium}$, $^{213}\text{bismuth}$, $^{77}\text{bromine}$, $^{18}\text{fluorine}$, $^{95}\text{ruthenium}$, $^{97}\text{ruthenium}$, $^{103}\text{ruthenium}$, $^{105}\text{ruthenium}$, $^{107}\text{mercury}$, $^{203}\text{mercury}$, $^{67}\text{gallium}$ and $^{68}\text{gallium}$.

Claim 64 (original) A pharmaceutical composition of claim 56 wherein the pharmaceutical agent is selected from the group consisting of doxorubicin, methoxymorpholinyl doxorubicin (morpholinodoxorubicin), adriamycin, cis-platinum, taxol, calicheamicin, vincristine, cytarabine (Ara-C), cyclophosphamide, prednisone, daunorubicin, idarubicin, fludarabine, chlorambucil, interferon alpha, hydroxyurea, temozolomide, thalidomide and bleomycin, and derivatives and combinations thereof.

Claim 65 (original) A pharmaceutical agent of claim 55 coupled to or complexed with a vehicle or carrier that is capable of being coupled or complexed to more than one agent.

Claim 66 (original) A pharmaceutical composition of claim 65 wherein the vehicle or carrier is selected from the group consisting of dextran, lipophilic polymers, HPMA and liposomes.

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Claim 67 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an amount effective to inhibit cell rolling.

Claims 68 - 71 (canceled)

Claim 72 (currently amended) A pharmaceutical composition of claim 49 [[48]] in an amount effective to inhibit metastasis.

Claim 73 (currently amended) A pharmaceutical composition of claim 49 [[48]] comprising the antibody multimer in an amount effective to inhibit growth and/ or replication of tumor cells, increase mortality of tumor cells, or increase the susceptibility of tumor cells to damage by anti-cancer agents.

Claim 74 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an amount effective to inhibit growth and/ or replication of leukemia cells, increase the mortality rate of leukemia cells or increase the susceptibility of leukemia cells to damage by anti-leukemia agents.

Claim 75 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an amount effective to increase the susceptibility of diseased cells to damage by anti-disease agents.

Claim 76 (original) A pharmaceutical composition of claim 49 comprising the antibody multimer in an amount effective to inhibit cell-cell, cell-matrix, platelet-matrix, platelet-platelet, and/ or cell-platelet aggregation, adhesion or complex formation.

Claim 77 (original) A pharmaceutical composition of claim 49 coupled to or complexed with an agent selected from the group consisting of anti-cancer, anti-metastasis, anti-leukemia, anti-disease, anti-adhesion, anti-thrombosis, anti-restenosis, anti-autoimmune, anti-aggregation, anti-bacterial, anti-viral, and anti-inflammatory agents.

Claim 78 (original) A pharmaceutical composition of claim 78 wherein the agent is an anti-viral agent selected from the group consisting of acyclovir, ganciclovir and zidovudine.

Claim 79 (original) A pharmaceutical composition of claim 49 wherein the antibody multimer is coupled to or complexed with a vehicle or carrier that is capable of being coupled or complexed to more than one agent.

Claim 80 (original) A pharmaceutical composition of claim 49 wherein the vehicle or carrier is selected from the group consisting of dextran, lipophilic polymers, HPMA, and liposomes.

Claims 81-97 (canceled)

Claim 98 (previously presented) A kit comprising at least one antibody multimer according to any one of claim 1, 4, 7, 27, 28, 117, 118, 138, and 139.

Claim 99 (previously presented) An antibody multimer of claim 4 wherein the multimer is a dimer, trimer or tetramer.

Claim 100 (previously presented) An antibody multimer of claim 99 wherein the multimer is a dimer.

Claim 101 (previously presented) A dimer of claim 100 wherein at least one of the first and second antigen binding fragments is selected from scFv fragments of Y1 and Y17.

Claim 102 (previously presented) A dimer of claim 100 wherein the first and second antigen binding fragments are linked by a disulfide bridge.

Claim 103 (previously presented) A dimer of claim 102 wherein the first and second antigen binding fragments are Y1-Cys-KAK.

Claim 104 (previously presented) A dimer of claim 100 wherein the first and second antigen binding fragments are linked by a polypeptide linker of 5 to 20 amino acids.

Claim 105 (previously presented) A dimer of claim 104 wherein the polypeptide linker comprises 5 amino acids.

Claim 106 (previously presented) A dimer of claim 105 wherein the polypeptide linker is Gly₄Ser.

Claim 107 (previously presented) An antibody multimer of claim 99 wherein the multimer is a trimer.

Claim 108 (previously presented) A trimer of claim 107 comprising three antigen binding fragments, wherein at least one of the antigen binding fragments is a Y1 scFv fragment or Y17 scFv fragment.

Claim 109 (previously presented) A trimer of claim 108 wherein the antigen binding fragments are linked by a polypeptide linker.

Claim 110 (previously presented) A trimer of claim 109 wherein the polypeptide linker comprises 1 to 5 amino acids.

Claim 111 (previously presented) An antibody multimer of claim 99 wherein the multimer is a tetramer.

Claim 112 (previously presented) A tetramer of claim 111 comprising four antigen binding fragments, wherein at least one of the antigen binding fragments is a Y1 scFv fragment or Y17 scFv fragment.

Claim 113 (previously presented) A tetramer of claim 112 wherein the antigen binding fragments are linked by a polypeptide linker.

Claim 114 (previously presented) A tetramer of claim 113 wherein the polypeptide linker comprises 1 to 5 amino acids.

Claim 115 (previously presented) A tetramer of claim 111 wherein the four antigen binding fragments form a complex through streptavidin-biotin association.

Claim 116 (previously presented) An antibody multimer of claim 99 comprising identical antigen binding fragments.

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Claim 117 (previously presented) An antibody multimer of claim 99 wherein the at least first or second antigen binding fragment or both comprises a first hypervariable region comprising SEQ ID NO: 8.